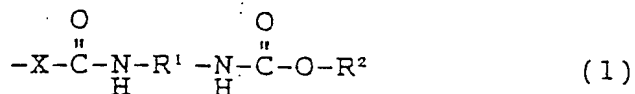


REMARKS

Claim 19 has been amended in order to correct an obvious grammatical error contained therein. No new matter has been added.

Claims 19-22, 24 and 25 have been rejected under 35 USC 103(a) as being unpatentable over Akiyoshi et al. Applicants respectfully traverse this ground of rejection and urge reconsideration in light of the following comments.

As stated previously, the instant invention is directed to a purified product of a polysaccharide containing a hydrophobic group which has a content of at least 80% by weight of the polysaccharide containing the hydrophobic group. The polysaccharide contains a group represented by -XH in which X is either an oxygen atom or a nitrogen-containing group represented by NY with Y being a hydrogen atom or a hydrocarbyl of 1-10 carbon atoms. 0.1-10 -XH groups per 100 monosaccharide units containing the polysaccharide are replaced by one or more hydrophobic groups represented by Formula (I)



, in which X is the same as above, R<sup>1</sup> is a hydrocarbyl having 1-50 carbon atoms and R<sup>2</sup> is a hydrocarbon group of 12-50 carbon atoms or a steryl group. The content of an impurity product, in which both of the NCO groups in the diisocyanate are reacted with the hydroxyl group-containing hydrocarbon having 12-50 carbon atoms or with a sterol, is not greater than 0.05% by weight.

The polysaccharide containing the hydrophobic group is obtained by a process comprising a first step of producing an isocyanate group-containing hydrophobic compound, wherein one mole of a hydroxyl group-containing hydrocarbon having 12-50 carbon atoms or of a sterol is reacted with a diisocyanate

represented by  $\text{OCN-R}^1\text{-NCO}$  in which  $\text{R}^1$  is a hydrocarbyl of 1-50 carbon atoms, a second process step of producing a polysaccharide containing a hydrophobic group composed of the hydrocarbon group of 12-50 carbon atoms or of the steryl group, wherein the isocyanate group-containing hydrophobic compound obtained in the first process step is reacted with one or more polysaccharides to form a reaction product and the reaction product is purified from the second process step using a solvent based on a ketone.

The high purity polysaccharide of the present invention can be utilized as a material for coating a drug-carrier enclosing a medicament due to its high purity and is particularly useful in the formation of liposomes. Conventional polysaccharide-based liposomes have problems in that impurities are present in the polysaccharide having a hydrophobic group that make up the liposomes and these impurities have a negative influence on the physical chemical stability, cell specificity and adaptability of the liposome or emulsion coated with the polysaccharide. The high purity polysaccharide of the present invention containing a hydrophobic group avoids the problems associated with conventional polysaccharides. It is respectfully submitted that the presently claimed invention is patentably distinguishable over the prior art cited by the Examiner.

The Akiyoshi et al reference discloses hydrophobic polysaccharide derivatives having palmitoyl or cholesterol moieties. The polysaccharide derivatives of Akiyoshi et al are purified by dialysis using a seamless cellulose tube. As pointed out previously, dialysis purification is not effective to separate unreacted polysaccharide molecules or byproducts, such as cholesterol dimers, from the reaction product, even though dialysis may be effected for separating small-size molecules capable of passing through the semipermeable membrane. Therefore, it cannot be assumed that this reference shows a purification technique for obtaining a polysaccharide as required by the present claims.

Moreover, the Akiyoshi et al reference also does not disclose the presently claimed requirement that the content of the impurity product in which both the NCO groups and the diisocyanate are reacted with the hydroxyl group-containing hydrocarbon having 12-50 carbon atoms or with the sterol is no greater than 0.05% by weight. As discussed above, one of the inventive features of the present invention is the low content of impurity contained therein. Therefore, it is respectfully submitted that the Akiyoshi et al reference does not show the presently claimed invention.

In order to further show the patentability of the presently claimed invention over the Akiyoshi et al reference, Applicants are enclosing herewith a Declaration Under 37 CFR 1.132. In the enclosed Declaration Under 37 CFR 1.132, an additional Comparative Example 2 is presented in which a cholesterol-substituted polysaccharide derivative of the Akiyoshi et al reference is prepared. The cholesterol-substituted polysaccharide derivative of Comparative Example 2 is to be compared with the polysaccharide derivative of the present invention prepared according to Example 1-3 in the present specification.

In Example 1-3 of the present specification, purification is carried out by reprecipitation using acetone with subsequent ultracentrifugation. With these purification steps, a cholesterol dimer is largely removed by the acetone/preprecipitation and unsubstituted pullulan is largely removed by the ultracentrifugation. As shown in Table 2 of the present specification, the pullulan cholesterol derivative of the present invention was obtained at a higher purity and the contents of both unsubstituted pullulan and cholesterol dimer were 0%.

In contrast to the present invention, the purification technique disclosed in Akiyoshi et al is based on reprecipitation with ethanol which is performed by procedures corresponding to that of Comparative Example 1 of the present specification, followed by dialysis. This procedure was

followed in Comparative Example 2 in the enclosed Declaration Under 37 CFR 1.132. As can be seen by the results of Comparative Example 2 in the Declaration, cholesterol dimer was present after reprecipitation with ethanol as opposed to the claimed requirement of reprecipitation with acetone. Also, by the employment of dialysis instead of ultracentrifugation as required by the present invention, unsubstituted pullulan was also found to be present. That is, the content of the cholesterol dimer was 0.5% by weight and the unsubstituted pullulan was 3.6 % by weight in the process of Akiyoshi et al. In contrast thereto, the polysaccharide composition of the present invention did not contain any of the impurities.

The hydrophobic group-containing polysaccharide of the present invention is of a very high purity and can be used for materials in medical use, such as a coating material for coating a drug-carrier enclosing medicaments. Although the Akiyoshi et al reference does disclose a hydrophobic group-containing polysaccharide, the purification technique shown in this reference cannot attain the high purity obtained by the present invention as evidenced by the result of Comparative Example 2 in the enclosed Declaration. Therefore, it is respectfully submitted that the presently claimed invention clearly is patentably distinguishable over this reference. An executed copy of the Declaration will be submitted to the Patent Office upon Applicants' representative's receipt of the same.

Reconsideration of the present application and the passing of it to issue is respectfully solicited.

Respectfully submitted,

  
Terryence F. Chapman

TFC/smd

FLYNN, THIEL, BOUTELL	Dale H. Thiel	Reg. No. 24 323
& TANIS, P.C.	David G. Boutell	Reg. No. 25 072
2026 Rambling Road	Ronald J. Tanis	Reg. No. 22 724
Kalamazoo, MI 49008-1631	Terryence F. Chapman	Reg. No. 32 549
Phone: (269) 381-1156	Mark L. Maki	Reg. No. 36 589
Fax: (269) 381-5465	Liane L. Churney	Reg. No. 40 694
	Brian R. Tumm	Reg. No. 36 328
	Steven R. Thiel	Reg. No. 53 685
	Sidney B. Williams, Jr.	Reg. No. 24 949

Encl: Declaration Under 37 CFR 1.132  
Postal Card

136.05/04